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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHOI, FRANK I	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 06/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/214,848	SEKINE, TERUAKI	
	Examiner	Art Unit	
	Frank I. Choi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/29/2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-27,31,32 and 34-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-27,31,32,34-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12,15-18,35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reasons:

A single claim which claims both a product and the method steps of using the product is indefinite under 35 U.S.C. 112, second paragraph. See Ex parte Lyell, 17 USPQ2d 1548 (Bd. Pat. App. & Inter. 1990) (claim directed to an automatic transmission work stand and the method steps of using it was held to be ambiguous and properly rejected under 35 U.S.C. 112, second paragraph). In this case, the claims are directed to activated autologous lymphocytes. However, the lymphocytes can only be "autologous" if the lymphocytes are administered to the person from whom they were taken or at the least used in vitro against infected cells from said person ; i.e., the claim inherently requires administration of the composition into the person who donated the lymphocytes or contact with infected cells from said person. As such, the claims contain both a product and the method steps of using the product. Further, claims 12,15-18 are also rejected under 35 U.S.C. 101 based on the theory that the claim is directed to neither a "process" nor a "composition of matter," but rather embraces or overlaps two different statutory classes of

invention set forth in 35 U.S.C. 101 which is drafted so as to set forth the statutory classes of invention in the alternative only. See ld. at 1551. See MPEP Section 2173.05(p)(II).

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 12, 15-18, 35 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alterative, under 35 U.S.C. 103(a) as obvious over Koenig et al.

Koenig et al. expressly discloses compositions comprising autologous lymphocytes from an AIDS patient activated with IL-2 and OKT3 which activated autologous lymphocytes at doses of 28×10^9, 12×10^9 and 13×10^9 were resuspended in normal saline and human serum albumin and reinfused into the patient for treatment of the patient's HIV infection falling within the scope of applicant's claims (Pg. 333, Abstract, Pgs. 333-335).

Alternatively, at the very least the claimed invention is rendered obvious within the meaning of 35 USC 103, because the prior art discloses products and uses that contain the same exact ingredients/components as that of the claimed invention. See In re Fitzgerald, 205 USPQ 594 (CCPA 1980). See also In re May, 197 USPQ 601, 607 (CCPA 1978). Although, Koenig et

al. appears to disclose the use of soluble OKT3 instead of solid phase OKT3, the claim is directed to a product not a process. As such, the burden is on Applicant to show that activated lymphocytes using solid OKT3 are different from activated lymphocytes using soluble OKT3.

Examiner has duly considered Applicant's arguments but deems them unpersuasive.

The use of the solid phase "anti-CD3 antibodies" is with respect to the process by which the autologous lymphocytes are activated. There is no indication from the product claims that the solid phase "anti-CD3 antibodies" are part of the composition or administered to the patient as part of the treatment method. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). As such, the fact that Koenig uses soluble OKT3 rather than solid phase OKT3 does not overcome the rejection.

Any difference in volume of activated lymphocytes between the prior art process and the process set forth in the composition claims does not overcome the rejection as the composition claims only require that activated autologous lymphocytes from a virally infected patient (other than cytomegalovirus) be present in the composition. Since the prior art expressly discloses a composition containing activated lymphocytes that was injected into the donating patient who was infected with HIV, the claimed composition is anticipated by the prior art notwithstanding that the process for proliferating and activating the autologous lymphocytes used soluble OTK3 rather than solid phase OTK3. Applicant's reliance on Tokoro et al. is misplaced as that reference indicated that the apoptosis occurred in TCR alpha negative mutant mice that did not

express TCR alpha beta antigen receptors. There is no indication that the results in said mutant mice have any relevance to the method disclosed in Koenig. Further, Tokoro et al. does indicate that viable cells were produced (See Tokoro et al., Pg. 1014, table 1). As such, even if relevant, the Tokoro et al. reference would appear to go to the volume of activated lymphocytes produced by the process. As such, neither the Tokoro et al. reference nor the Sekine et al. reference provides evidence that the claimed composition is different from the prior art composition.

Applicant argues that Koenig et al. teaches away from the claimed method for treating a viral infection. However, the method disclosed in Koenig et al. was effective against a viral infection, i.e. viral strains of HIV that were susceptible to the nef-specific T-lymphocyte (See Page 333). As such, the fact that the method in Koenig was not effective against other viral strains of HIV does not preclude the determination that the Koenig method anticipates the claimed composition. Further, Koenig et al. does not teach away from using the claimed method in treating viral infections as Koenig et al. indicated that the activated lymphocytes were effective against certain viral strains of HIV, that the patient's clinical deterioration might have been more accelerated without the treatment and the negative outcome may have been the result of induction and secretion of virus-enhancing cytokines, release of free virions from infected cells lysed by the lymphocytes and dissemination to other tissue compartments, inappropriate dosing of the lymphocytes and/or selection of non-susceptible variants possibly due to rapid turnover of viral population *in vivo* (See Koenig et al, Discussion, pages 332-334). Even if Koenig et al. could be construed as teaching away, any such teaching away would be limited to the factual situation disclosed in Koenig et al., i.e. the HIV strains not susceptible to the nef-specific T-lymphocytes. This supported by the disclosure in Koenig et al. which indicated that adoptive transfer of human cytomegalovirus specific T-lymphocytes inhibited cytomegalovirus

and since the viral load is much less in cytomegalovirus patients as compared to individuals chronically infected with HIV, the risk of selection of cytomegalovirus variants would be reduced (See Koenig et al., Page. 332). In any case, since the viral infection set forth in the claims is not required to be an HIV infection, any such teaching away is not sufficient to overcome the rejection. Further, based on the above, one of ordinary skill in the art would expect that by monitoring the HIV viral strains and adjusting the activated T-lymphocytes to recognize the HIV viral strains, nef-type or other wise, preferably in conjunction with drugs which inhibit replication, that the method disclosed in Koenig et al. would be effective in treating HIV infection per se. (See e.g. Koenig et al., pages. 333,334).

Examiner notes that the withdrawal of the rejection of the method of use claims 14, 23-27, 37 is not due to Applicant's arguments and is solely based on the fact that said claims require the use of solid phase anti-CD3 antibodies in the process of making limitations contained therein whereas the process disclosed in Koenig uses soluble anti-CD3 antibodies.

Claims 12-27, 31, 32, 34-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ochoa et al. (US Pat. 5,296,353) in view of Babbit et al. (US Pat. 5,766,920), Ochoa et al. (U.S. Pat. 5,443,983), the acknowledged prior art, Wallace et al., Santamaria et al. and Sekine et al.

Ochoa et al. (US Pat. 5,296,353) teach activation of autologous T-lymphocytes with anti-CD3 (soluble or solid phase bound), such as OKT3, and cytokines, including IL-2, for treatment of cancers and diseases of viral etiology such as those caused by HIV, cytomegalovirus and Epstein Barr virus (See entire document, especially, Column 3, lines 32-50, Column 7, lines 54-68, Column 8, lines 1-35, Column 11, lines 29-54, Column 12, lines 15-54).

Babbitt et al. teach activation of autologous T-lymphocytes (including that taken from peripheral blood of virally infected patients) with OKT3 and cytokines, including IL-2, for treatment of tumors or viral pathogens, including herpesvirus (herpes simplex virus and cytomegalovirus), Epstein Barr virus and HIV (See entire document, especially, Column 2, lines 22-68, Column 3, Column 7, lines 40-49, Column 20, lines 53-68, Column 21, lines 1-16). It is disclosed that solid phase OKT3 may be used but that soluble OKT3 is preferred (Column 12, lines 1, 2).

Ochoa et al. (U.S. Pat. 5,443,983) teach a method of developing LAK activity in lymphocytes comprising contacting lymphocytes with IL-2 and an anti-CD3 antibody and a method of administering the same suspended in a phosphate buffered saline supplemented with human serum albumin to an AIDS patient (Column 11, lines 49-68, Column 12, lines 1-50, Claims 1-8).

Applicant acknowledges that T-cells are involved in cellular immunity against cancer and viruses (Specification, Pgs. 1, 2). Further, it is acknowledged that lymphocytes, including T-cells and NK cells, can be activated and stimulated by IL-2 and that lymphocytes can be activated and stimulated with IL-2, with or without CD3 antibodies, including against viruses, such as, EBV and CMV (Specification, pgs. 3,4).

Wallace et al. disclose activation of T-cell precursors from the circulation of seropositive individuals with IL-2 and that the same are effective against autologous EBV transformed cells (Page 1012, Abstract).

Santamaria et al. disclose cytomegalovirus primed peripheral blood mononuclear cells from seropositive subjects which are stimulated by anti-CD3 coated onto polystyrene beads plus interleukin-2 and that polystyrene coated with antibodies can induce the long term-growth of

antigen specific T-cell lines in the absence of specific antigen and feeder cells (Page 1, Abstract, Pages 4-7).

Sekine et al. discloses that cultivation of T lymphocytes from peripheral blood lymphocytes with immobilized anti-CD3 (OKT3) and IL-2 induces a rapid proliferative response and that the immobilized form of anti-CD3 proved better for expansion than soluble anti-CD3 (Page 73, Summary, Page 74, Page 77, Discussion).

The prior art discloses compositions, methods of preparing and methods of using activated autologous lymphocytes which are derived from virally infected patients and activated and proliferated by the combination of anti-CD3 antibodies in soluble or solid phase and interleukin –2, where the viral infection can be HIV, cytomegalovirus and Epstein Barr virus. The difference between the prior art and the claimed invention is that the prior art does not expressly disclose excluding cytomegalovirus-infected patients or the use of anti-CD3 in solid phase. However, the prior art amply suggests the same as the prior art discloses the activation of autologous lymphocytes which can be used to treat viral infections, including viral infections other than cytomegalovirus, such as herpes simplex and Epstein Barr virus, which lymphocytes are activated by interleukin-2 and anti-CD3; that the use of solid phase anti-CD3 results in better proliferation than soluble anti-CD3; and the suspension of lymphocytes activated with interleukin-2 and anti-CD3 which are suspended in phosphate buffered saline and albumin. As such, it would have been well within the skill of one of ordinary skill in the art to prepare activated autologous T-lymphocytes from patients having viral infections other than cytomegalovirus, with the expectation that the activated autologous T-lymphocytes would be effective against said viral infections. Further, it would have been well within the skill of one or ordinary skill in the art to use solid phase anti-CD3 rather than soluble anti-CD3 with the

expectation that suitable numbers of activated lymphocytes could be obtained at a faster rate. Finally, it would have been well within the skill of one of ordinary skill in the art to administer the activate autologous lymphocytes in a carrier containing phosphate buffered saline and albumin with the expectation that the same would be a suitable carrier.

Applicant's arguments have been duly considered but they are deemed unpersuasive in light of the new grounds of rejection. However, to the extent Applicant's arguments are applicable to the one or more of the prior art cited above, the following applies:

The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 208 USPQ 871 (CCPA 1981).

Applicant argues that none of the references disclose, teach or suggest the use of lymphocytes collected from the blood of a virally infected patient. However, the claims do not require that lymphocytes must be collected from the blood of a virally infected patient. In any case, the combined teachings of the prior art, as indicated above, do teach and suggest using lymphocytes collected from a virally infected patient, including lymphocytes collected from blood. See discussion of Babbit et al. (US Pat. 5,766,920), Wallace et al. and Santamaria et al. above.

Applicant makes a general argument that Santamaria is directed to long term studies, and concludes on this basis that there is nothing in Santamaria's disclosure that would suggest or motivate one of ordinary skill in the art to use autologous T lymphocytes derived from virally infected patients in combination with the disclosure of the other references. Applicant, however,

provides no evidence that one of ordinary skill in the art would conclude that the process in Santamaria is limited to use in long term studies or that long term cultivation or use in long term studies precludes the use of the activated lymphocytes in a treatment method. The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness."). Since the activation of autologous lymphocytes from virally infected patients with solid phase anti-CD3 and interleukin-2 is suggested by one or more of the other prior art, one of ordinary skill in the art would expect that the technique disclosed in Santamaria would suitable for use in preparing activated autologous lymphocytes for use in treating virally infected patients.

Koenig et al. is not part of the rejection herein. As discussed above, Koenig et al. does not teach away from the claimed invention and even if it could be concluded that Koenig et al. teaches away any such teaching away would be limited to specific fact situation in Koenig et al. and not viral infections per se. In any case, since none of the claims specifically require the viral infection to be an HIV infection, Applicant's citation to Koenig et al. is not sufficient to overcome the rejection herein.

Examiner notes that although Babbit et al. discloses that soluble OKT3 is preferred over solid phase OKT3, disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi, 169 USPQ 423 (CCPA 1971). "A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." In re Gurley, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994) (The invention was directed to an epoxy impregnated

fiber-reinforced printed circuit material. The applied prior art reference taught a printed circuit material similar to that of the claims but impregnated with polyester-imide resin instead of epoxy. The reference, however, disclosed that epoxy was known for this use, but that epoxy impregnated circuit boards have "relatively acceptable dimensional stability" and "some degree of flexibility," but are inferior to circuit boards impregnated with polyester-imide resins. The court upheld the rejection concluding that applicant's argument that the reference teaches away from using epoxy was insufficient to overcome the rejection since "Gurley asserted no discovery beyond what was known in the art." 31 USPQ2d at 1132.). In any case, the prior art also discloses the advantages of using solid phase anti-CD3. See discussion of Santamaria et al. and Sekine et al. above.

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier number for accessing the facsimile machine is 571-273-8300.

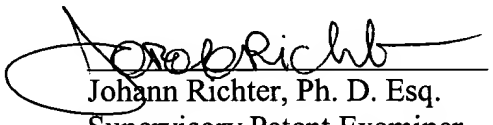
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Choi whose telephone number is (571)272-0610. Examiner maintains a flexible schedule. However, Examiner may generally be reached Monday-Friday,

8:00 am – 5:30 pm (EST), except the first Friday of the each biweek which is Examiner's normally scheduled day off.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Mr. Johann Richter, can be reached at (571)272-0646. Additionally, Technology Center 1600's Receptionist and Customer Service can be reached at (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Frank Choi
Patent Examiner
Technology Center 1600
June 8, 2006



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